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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 10/009,584      | 05/21/2002  | David M. Livingston  | 20363-012           | 1758             |

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EXAMINER

GUZO, DAVID

| ART UNIT | PAPER NUMBER |
|----------|--------------|
|          | 1636         |

DATE MAILED: 05/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

|                 |                        |  |
|-----------------|------------------------|--|
| Application No. | 10/009,584             |  |
| Examiner        | Art Unit<br>David Guzo |  |
|                 | 1636                   |  |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) Responsive to communication(s) filed on 08 April 2004.
- 2a) This action is FINAL.                            2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) Claim(s) 1-7 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 1-7 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on 21 May 2002 is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) All    b) Some \* c) None of:
  1. Certified copies of the priority documents have been received.
  2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) Notice of References Cited (PTO-892)
- 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 2/1/02.
- 4) Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) Notice of Informal Patent Application (PTO-152)
- 6) Other: \_\_\_\_\_.

**Detailed Action**

Applicant's election of Group I, Claims 1-7 in the Paper received 4/8/04 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below or on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Specifically, an amino acid sequence (Asp-Ala-Ala-Ile-Arg-Ser) appears on page 18.

Applicant must comply with the sequence rules, 37 CFR 1.821 - 1.825. Applicant is requested to return a copy of the attached Notice to Comply with the reply. Any reply that does not comply with the Sequence Rules will be considered non-responsive. However, the nature of the non-compliance with the Sequence Rules has not precluded an examination of the application on the merits, the results of which are communicated below.

**Priority**

Priority for the embodiments recited in claims 3 and 7 is granted back to the filing of the PCT document (PCT/US00/15325, filed 6/2/2000) because the provisional application 60/137,625 lacks written description support for these embodiments.

**35 USC 102 Rejections**

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-2, 4-5 are rejected under 35 U.S.C. 102(a) as being anticipated by Bhattacharya et al.

Applicants claim a method for identifying a compound that modulates a transcriptional response to hypoxia in a cell (which can be a cultured cell), said method comprising contacting the cell with a candidate compound, subjecting the cell to hypoxic conditions and assessing a transcriptional response of the cell to the hypoxic conditions. The transcriptional response is expression of a reporter gene under control of a hypoxia-responsive promoter. With regard to claim 4, it is noted that the claim still includes all of the embodiments of claim 2 (including use of a reporter gene under control of a hypoxia-responsive promoter) and only recites a further limitation of one embodiment of claim 2 (the use of different endogenous hypoxia-responsive genes in the method of claim 2). Therefore claim 4 is included in this rejection.

Bhattacharya et al. (Cited by applicants, Genes and Development, 1999, Vol. 13, pp. 64-75, see whole article, particularly the Abstract, the first paragraph on p. 64 and the paragraph bridging pp. 68-69 and Fig. 5C) recites a method for identifying a compound that modulates a transcriptional response to hypoxia in a cultured cell (Hep3B cell line), said method comprising contacting the cell with a candidate compound (p35srj), subjecting the cell to hypoxic conditions (induced by deferoxamine) and assessing a transcriptional response to the hypoxic conditions. The transcriptional response is expression of a reporter gene encoding luciferase, under control of a hypoxia responsive promoter (the vascular endothelial growth factor (VEGF) promoter), in response to the hypoxic conditions. Bhattacharya et al. therefore teaches the claimed invention.

Claims 1-2 and 4-5 are rejected under 35 U.S.C. 102(a) as being anticipated by Ebert et al.

Applicants' invention is as described above.

Ebert et al. (Cited by applicants, Mol. Cell. Biol., July 1998, Vol. 18, No. 7, pp. 4089-4096, see whole article, particularly the Abstract, pp. 4092-4093 and Fig. 7) recites a method for identifying a compound that modulates a transcriptional response to hypoxia in a cultured cell (i.e. Hepa-1 cells), said method comprising contacting the cell with a candidate compound (i.e. E1A protein), subjecting the cell to hypoxic conditions and assessing a transcriptional response to the hypoxic conditions. The transcriptional response is expression of a reporter gene under control of a hypoxia-

responsive promoter (the LDH-A promoter) to the hypoxic conditions. Ebert et al. therefore teaches the claimed invention.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 3 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Bhattacharya et al.

Applicants invention is as described above in the rejection of claims 1-2 and 4-5 over Bhattacharya et al. Additionally, in claim 3 applicants recite that the reporter can be luciferase and in claim 7, applicants recite that the hypoxic conditions can be induced by deferoxamine.

Bhattacharya et al. (Cited above, see whole article, particularly the Abstract, the first paragraph on p. 64 and the paragraph bridging pp. 68-69 and Fig. 5C) recites the instantly claimed method wherein the reporter used is luciferase and the hypoxic conditions are induced by addition of deferoxamine. Bhattacharya et al. therefore teaches the claimed invention. This rejection is made under 35 USC 102(b) because priority for the subject matter recited in claims 3 and 7 is granted back to the filing date of the PCT parent (6/2/00).

Claims 1-5 are rejected under 35 U.S.C. 102(b) as being anticipated by Arany et al.

Applicants invention is as recited above.

Arany et al. (Cited by applicants, PNAS, 1996, Vol. 93, pp. 12969-12973, see whole article, particularly the Abstract, the paragraph bridging pp. 12971-12972, Fig. 3-4 and the first paragraph in the Discussion section) recites a method for identifying a compound that modulates a transcriptional response to hypoxia in a cultured cell (Hep3B cells), said method comprising contacting the cell with a candidate compound (i.e. E1A), subjecting the cell to hypoxic conditions and assessing a transcriptional response to the hypoxic conditions. The transcriptional response is expression of the reporter gene encoding luciferase, under control of the hypoxia-responsive promoter (erythropoietin promoter/enhancer), in response to the hypoxic conditions. Arany et al. therefore teaches the claimed invention.

Claims 1, 2, 4 and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Fandrey et al.

Applicants invention is as described above.

Fandrey et al. (Biochem. J., 1994, Vol. 303, pp. 507-510, see whole article, particularly the Abstract; the first three paragraphs of the "Materials and Methods" section and Fig. 1) recites a method of identifying a compound that modulates a transcriptional response to hypoxia in a cell (cultured cell line HepG2), said method comprising contacting the cell with a candidate compound (i.e. H<sub>2</sub>O<sub>2</sub> or menadione),

subjecting the cells to hypoxic conditions and measuring a transcriptional response of the cell to the hypoxic conditions. The transcriptional response is the expression of a endogenous hypoxia-responsive gene (erythropoietin). Fandrey et al. therefore teaches the claimed invention.

### **35 USC 112, 2<sup>nd</sup> Paragraph Rejections**

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 (and dependent claims) are vague in that while applicants recite a method for identifying a compound that modulates a transcriptional response to hypoxia in a cell wherein the method involves assessing a transcriptional response of the cell to the hypoxic conditions, the claimed method does not have a step(s) which compares the transcriptional response to the candidate compound with a control response or standard. Without a comparison to a control of some kind, it is impossible to assess whether the candidate compound has any effect (over control levels) on a cellular response to hypoxia.

Claim 4 is vague in the recitation of the term “ortransferrin”. Possible applicants mean to recite “or transferrin”. Claim 4 is also vague in that applicants have not spelled out the abbreviated terms “iNOS” and “ALDA”.

Claim 7 is vague in the phrase "...cells are exposed induced by deferoxamine...".

Insertion of the word "are" between "exposed" and "induced" would be remedial.

### **Miscellaneous**

In all future responses where amendments to the claims are presented, applicants must present all of the claims (including canceled claims) in numerical order in the claim listing, i.e. the status of all of the claims ever presented in the application must be listed in numerical order (See 37 CFR 1.121(c)).

Claim 6 is free of the prior art because the art does not teach or render obvious the claimed method for identifying compounds that modulate a transcriptional response to hypoxia wherein said method takes place *in vivo* and involves assessing a transcriptional response of cells to the hypoxic conditions in the presence of a test compound.

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Guzo, Ph.D., whose telephone number is (571) 272-0767. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 5:30 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D., can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for

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published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David Guzo  
April 28, 2004

  
DAVID GUZO  
PRIMARY EXAMINER

**NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES**

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 CFR 1.821 - 1.825 for the following reason(s):

1. This application clearly fails to comply with the requirements of 37 CFR 1.821 - 1.825. Applicant's attention is directed to these regulations, published at 1114 OG 29, May 15, 1990 and at 55 FR 18230, May 1, 1990.
2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 CFR 1.821(c).
3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 CFR 1.821(e).
4. A copy of the "Sequence Listing" in computer readable form has been submitted; however, the content of the computer readable form does not comply with the requirements of 37 CFR 1.822 and/or 1.823, as indicated on the attached copy of the marked-up "Raw Sequence Listing."
5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A substitute computer readable form must be submitted as required by 37 CFR 1.825(d).
6. The paper copy of the "Sequence Listing" is not the same as the computer readable form of the "Sequence Listing" as required by 37 CFR 1.821(e).
- 7.

Other:

Applicant must provide:

- An initial or substitute computer readable form (CRF) copy of the "Sequence Listing"
- An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification
- A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 CFR 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d)

For questions regarding compliance with these requirements, please contact:

For Rules Interpretation, call (703) 308-1123  
For CRF submission help, call (703) 308-4212  
For PatentIn software help, call (703) 557-0400